

CYTOPLASMIC RECEPTORS FOR GLUCOCORTICOIDS IN INTESTINE OF SUCKLING RATS. Susan J. Renning, Phillip L. Ballard, and Norman Kretschmer, Depts. of Ped., Stanford Univ. Med. Ctr., Stanford, and Univ. of California, San Francisco, California

Previous studies have shown that, in the intact animal, administration of glucocorticoid hormones can precociously simulate the various enzymic and morphological changes that normally occur in the rat intestine at weaning. In order to determine if these hormones act directly on intestinal cells, a search was made for cytoplasmic receptor proteins which are characteristic of target tissues. When incubations were attempted at 4° using ³H-dexamethasone (40 nM) and intestinal cytosol from 18-day-old rats, specific binding was observed but was unstable, being maximal after 1-2 hours then declining rapidly. This problem was overcome by using intestinal rings rather than isolated cytosol; under these conditions it was shown that the specific binding component is saturable and has an apparent dissociation constant of 9.3 ± 2.6 nM and a concentration of 0.24 ± 0.01 pmoles/mg protein in both jejunum and ileum. In a developmental study, the concentration of binding sites was found to decline gradually; from 0.31 ± 0.06 pmoles/mg protein at 5 days to 0.14 ± 0.02 pmoles/mg protein in adults. The presence of these cytoplasmic receptors during the suckling period is taken as evidence that glucocorticoids do act directly on the intestine; but, since there is no dramatic change in their concentration with age, it is unlikely that they play a primary role in the regulation of responsiveness of intestinal tissue to these hormones.

GASTROESOPHAGEAL MANOMETRY IN CHILDREN WITH GASTROESOPHAGEAL REFLUX. John J. Herbst and Dale G. Johnson. Departments of Pediatrics and Surgery, Univ. of Utah Col. of Med., Salt Lake City, Utah.

Gastroesophageal reflux (GE reflux) is frequently a serious disorder in children. Esophageal motility and pH (EMPH) studies were performed on 52 children who were not improving after at least 2 weeks of intensive medical treatment of GE reflux. Postoperative studies were also obtained on the 32 patients who eventually had surgery for reflux. An esophageal hiatal hernia was demonstrated in 41 of the patients. In 9, GE reflux was not demonstrated during the initial radiographic examination. Significant congenital abnormalities were identified in 11 children operated upon for GE reflux. Although there is a decreased pressure in the esophageal high pressure zone (HPZ) in the adult with GE reflux, HPZ pressures were normal for age in our patients. HPZ pressures did not increase after surgery. The mean change in patients with good results was +1.2 mm Hg, and +0.3 mm Hg in patients with fair results (reflux only during EMPH studies) or poor results (return of symptoms). Successful surgical repair of GE reflux in adults has been associated with an increased HPZ pressure. EMPH studies are more sensitive than roentgenography in detecting reflux in children. GE reflux in the child differs from the adult in that there is a high incidence of congenital abnormalities, HPZ pressures are not depressed, and a rise in HPZ pressure is not correlated with a successful surgical repair.

ENZYM REPLACEMENT THERAPY: DIRECTING EXOGENOUS ENZYME TO THE LIVER. Neil A. Holtzman, Gloria F. Bell, Mark J. Krantz, Hans H. Liu, Yuan C. Lee. The Johns Hopkins University, Departments of Pediatrics and Biology, Baltimore, Maryland.

Mammalian liver possesses sites, not shared by other organs, which bind several glycoproteins whose terminal sugars are galactose. Such proteins are taken up rapidly--and almost exclusively--by the liver following intravenous administration (Morell, et al. *J. Biol. Chem.* 246:1461, 1971). We determined whether the coupling of p-aminophenyl-thio-derivatives of either galactose or glucose to purified Aspergillus amylase could increase binding of the enzyme to liver *in vitro* and *in vivo*. The enzymes to which sugar was coupled (gal-amylase or glu-amylase) had 60% of the enzyme activity of the unmodified amylase. Employing the assay of van Lenten and Ashwell (*J. Biol. Chem.* 247:4633, 1972) the greatest affinity for the binding site on liver cell membrane was observed with gal-amylase; over 50 times as much glu-amylase was required for comparable binding. Unmodified amylase did not bind even when 10⁵ times as much was used. Mice were injected intravenously with either unmodified ¹²⁵I-amylase, ¹²⁵I-gal-amylase or ¹²⁵I-glu-amylase and sacrificed 5-15 minutes later. The proportion of radioactivity found in whole liver was highest for gal-amylase, intermediate for glu-amylase and least for unmodified amylase. It remains to be determined whether the rapid uptake of gal-amylase is associated with diminished immune response and to what extent its enzyme activity persists in the liver.

FAT ABSORPTION IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS. Lorne Katz, Richard Hamilton, Res. Inst., Hosp. for Sick Children, Dept. of Ped., Univ. of Toronto, Toronto, Canada.

We studied 15 infants, birth weight less than 1300 grams, during their first 2 months of life. Fecal fat excretion (% of intake) was 20.1 ± 6.3 (m ± sd) at age 10-14 days and 26.4 ± 8.0 at 3 weeks. In 10 infants not given calcium supplements, fat excretion at 6-8 weeks declined significantly (p < .01) to 11.6 ± 5.6 . In 5 infants given oral Ca supplements (147 mg Ca/Kg/day), beginning at age 3 weeks, fat excretion at 6-8 weeks was 20.9 ± 7.0 , greater (p < .05) than in nonsupplemented infants. At age 2 weeks mean maximal postprandial intraluminal total bile salt concentration measured by TLC was 1.5 mEq/L; 8/10 were below the critical micellar concentration (CMC). There were no free bile salts (FBS) and minimal amounts of glycine conjugates. At 2 months the bile salt concentrations were increased; 8/10 were above the CMC. There were no FBS and increased glycine conjugates. There was a significant (p < .01) correlation between intraluminal bile salt concentration and fecal fat excretion (r = -.67). Mean lipase activity (µM/ml/min) in postprandial duodenal juice was 9.3 at 2 weeks and 26.0 at 2 months, but since monoglycerides, diglycerides were identified consistently in duodenal contents some effective lipolysis was occurring. We conclude that mild fat malabsorption in VLBW infants at 2-3 weeks of age, which can be attributed in part to deficient intraluminal bile salt concentrations, improves to approach adult capacity by age 2 months. Oral Ca supplements impair fat absorption in these infants.

MODULAR FORMULA FOR WEANING INFANTS FROM TOTAL PARENTERAL NUTRITION (TPN). W.J. Klish, J.T. Rodriguez, E. Potts, G. Ferry, and B.L. Nichols. Section of Nutrition and Gastroenterology, Department of Pediatrics, Baylor College of Medicine, Houston, Texas 77025.

Frequently, infants with chronic diarrhea and failure to thrive require TPN to overcome the intestinal absorptive defect. Weaning from TPN without exacerbation of diarrhea is difficult. We have developed a formula which can be structured to challenge the intestine sequentially with the various nutrient modules and concentrations. The Core formula is composed of whole casein and minerals calculated to deliver adequate electrolytes when used in a concentration of 3 gms % protein. To this protein Core, fats and sugars can be added as needed and tolerated by the patient. When weaning from TPN, modules are added in 1 gm % increments every 12 hrs. starting with protein, fat and then carbohydrate. When the composition equals 3 gm % Core mix, 3.5 gm % fat and 6 gm % carbohydrate and this is tolerated for 1 week, the patient is switched to a proprietary formula which most closely matches. If a concentration is reached that causes diarrhea, it is maintained or slightly reduced until intestinal tolerance develops. In the past three years, more than 75 patients have been weaned to oral feedings in this manner with no difficulty. Work supported by: Ross Laboratory, David Underwood Trust, USPH RR-00188, and AM-05721-01.

MORPHOLOGIC BASIS FOR GLUCOSE MALABSORPTION IN INFANTS WITH ACQUIRED MONOSACCHARIDE INTOLERANCE (AMI). W.J. Klish, J.T. Rodriguez, P. Soriano, T.L. Huang, G. Ferry, and B.L. Nichols Section of Nutrition and Gastroenterology, Baylor Col. of Med., Houston, Texas 77025.

Infants with AMI have chronic acidic diarrhea secondary to malabsorption of all carbohydrates resulting in profound malnutrition. Four patients with AMI were studied by an intestinal perfusion technique. A triple lumen tube with a Pediatric Crosby capsule at the tip was introduced into the jejunum. A 10% glucose solution was infused through a proximal site 30 cm from the collecting point. 1% polyethylene glycol was added as a non-absorbable marker. Samples were obtained every 15 minutes and glucose absorption rate was calculated. After the perfusion, a jejunal biopsy was obtained for histology and disaccharidase assay.

Glucose absorption increased from 9.2 to 17.3 mg/min after 1 month rehabilitation. Villous length increased with recovery. Lactase, sucrose and maltose enzymes remained low.

A linear relationship exists between glucose absorption and villous length. This implies that impaired glucose absorption is related to decreased mucosal surface area. Work supported by: Ross Laboratory, David Underwood Trust, NASA Contract 90059, USPH RR-00188 and AM-05721-01.